REMARKS

Claims 1-4, 6, 12-14, 17, 18, and 26-27 are pending in the instant application. Claim 1 was amended in the prior response which was not entered into the record. Therefore, Claim 1 is indicated herein to be amended. Claims 28 and 29 have been added. The claims are supported throughout the specification, for example in paragraph 89 of the PCT specification, and page 21, lines 5-13 of the translated specification.

The Advisory Action has maintained the rejections of the prior Office Action. Applicant requests that the response filed on October 8, 2009 be considered in conjunction with the comments and amendments provided herein. Applicant submits that the claims are not obvious in view of any combination of references set forth in the Office Action and respectfully requests that a Notice of Allowability be issued in the case in view of the forgoing amendments and the following arguments.

The Office Action has rejected Claims 1-4, 6, 17-18 and 26-27 under 35 U.S.C. 103(a) for allegedly being unpatentable over Kosaka et al. (Exp Cell Res 245: 245-251, 1998), and Tropepe et al. (Sc. 287: 2032-2036, 2000), in view of Pardo et al. (Brain Res 818: 84-95, 1999), and further in view of Lee et al (Theriogenology 44: 71-83, 1995) and Samarut et al., (US Patent number 6,500,668, dated 31 December 2002), as evidenced by Reynolds et al. (Sc. 255: 1707-1710, 1992) and Kitchens et al. (J. Neurobiol 25: 797-807, 1994).

The basic technical idea of the claims of the present application is to "differentiate pluripotent stem cells derived from iris pigmented epithelial cells to myocardial cells". However, none of the references cited in the outstanding Office Action teach or suggest such a technical idea. Therefore, the rejection should be withdrawn.

First, none of the references teach or suggest inducing differentiation to myocardial cells. Particularly, Lee, Samarut, and Kitchens, which were newly added in the rejections in the final Office Action, only teach the effects of serums or factors

claimed in other types of cultures. Specifically, Lee teaches **increasing the number of blastocysts** and the development of embryo *in vitro*. Samarut teaches the culture of bird **embryonic stem cells** using a culture medium comprising fetal bovine serum and chicken serum. Kitchens teaches culturing of neuronal cells. The effects of serum and growth factors in these substantially different culture systems provides no indication as to how the serum and growth factors would act alone in the instant culture methods, never mind in combination. It is well known in the art that combinations of growth factors can produce an outcome that is distinct from a simple additive effect. Therefore, it is impossible to arrive at an idea of "obtaining myocardial cells by culturing pluripotent stem cells in a culture medium containing fetal calf serum, avian serum, EGF, and FGF2 for one to two months" even if the references were considered in combination.

Tropepe discloses culturing of cells by a neurosphere method, which is relevant to the floated coagulated mass culturing technique of the invention of the present application. However, Tropepe uses an isolated pigment cell (PCM) derived from a ciliary margin of a mouse, which is different from the iris pigmented epithelial cells (IPE), as claimed, that serve as the material (original cells) in the method of the present invention for producing cells of a different type, more specifically, myocardial cells as claimed.

Further, Tropepe neither discloses nor suggests that the culturing method disclosed therein is applicable to culturing of iris pigmented epithelial cells (IPE) which are different from the isolated pigment cells cultured by Tropepe. Further, Tropepe suggests nothing regarding using a culture medium containing an N2 supplement and at least one of FGF, LIF, and SCF, as recited in amended claim 1.

Moreover, as noted by Kosaka, different cells are appropriately cultured using different culturing methods, as discussed in the prior response to Office Action. It is disclosed in Kosaka that an iris pigmented epithelial cell (IPE) culturing methods and a retinal pigment epithelium (RPE) culturing methods are substantially different from each other.

Furthermore, based on the descriptions in Tropepe, a cultured pigment cell, obtained by isolating a pigment cell (PCM) from a ciliary margin of a mouse and then cultured by the neurosphere method, **can only differentiate to cells that are derived from a retinal stem cell**, not a myocardial cell as claimed.

The instantly claimed invention includes steps to obtain myocardial cells, which are clearly distinct from retinal cells, from an iris pigmented epithelial cell (IPE) taken from an eye of an animal. Therefore, even though Tropepe discloses culturing of cells by the neurosphere method, it is impossible, from the description therein, to arrive at the methods of the instantly claimed invention for inducing differentiation of IPE cells to myocardial cells, which are a completely different type of cell from the original cell type. The same applies for the other references.

In the Advisory Action dated November 3, 2009, the Examiner states that "Furthermore, Applicant is arguing limitations that are not present or required in the current claims. For example the differences in cell types IPE versus RPE, and the selection of culture medium to deal with the differences, is not relevant to the instantly claimed invention". However, claim 1 of the present application clearly recites that iris pigmented epithelial cells are used as the material for producing the tissue cells more specifically, myocardial cells.

Applicant respectfully disagrees. Tropepe teaches the use of a pigment cell (PCM) isolated from a ciliary margin of a mouse, which is different from the iris pigmented epithelial cells claimed. Further, Applicant asserts that it is difficult to arrive at a technical idea of obtaining myocardial cells from the iris pigmented epithelial cells IPE as recited in claim 1 by the method disclosed in Tropepe, based on the description disclosed in Kosaka, which teaches that iris pigmented epithelial cell (IPE) culturing methods are substantially different from a retinal pigment epithelium (RPE) culturing methods.

Moreover, claim 1 has been amended to recite "the culturing medium comprising serum free medium, an N2 supplement, and at least one factor selected

from the group consisting of fibroblast growth factor (PGF), leukemia inhibitory factor (LIF), and stem cell factor (SCF)" which further differentiates the instantly claimed method from the cited art.

Thus, Applicant asserts that the claims set forth as above are not obvious in view of the cited art in any possible combination and that the pending application is in condition for allowance.

Extension of Time and Fee Authorization

The Commissioner is hereby authorized to charge Deposit Account 04-1105 the fee for a one (1) month extension of time and a Request for Continued Examination referencing Docket No. 64614(70904). It is believe that there is no further fee due with this response. However, if a fee is due, with this paper or any other paper filed by this firm in relation to this application, the Commissioner is hereby authorized to charge the Deposit Account referencing the Docket No. Credit of overpayment is respectfully requested.

Dated: December 11, 2009

Respectfully submitted,
Electronic signature: /Colleen McKiernan, Ph.D./
Colleen McKiernan, Ph.D.
Registration No.: 48,570
EDWARDS ANGELL PALMER & DODGE LLP
P.O. Box 55874
Boston, Massachusetts 02205
(617) 517-5555
Attorneys/Agents For Applicant